

### REMARKS

Favorable reconsideration is respectfully requested.

The claims are 13-22.

The above amendment makes self-explanatory minor amendments to the claims.

With regard to the rejection of claims 13-22 on the ground of obviousness-type double patenting over claims 1-8 of US 6,228,994, there is submitted herewith an appropriate Terminal Disclaimer.

Claims 13-15 and 20-22 have been rejected under 35 U.S.C. 102(b) as being anticipated by Vince et al. (Biochemistry, 17, 5489-5493) (1978).

The rejection is respectfully traversed.

As is clear from the title, abstract and description on page 5491, left column, lines 20-34, Vince et al. disclose a two-step method for labeling the A site of a ribosome by (1) covalently linking a photoaffinity labeling puromycin analogue N-(2-nitro-4-azidophenyl)-L-lysinyl puromycin aminonucleotide (NAP-Lys-PAN) with the ribosome by irradiation, and (2) then forming an ester bond by transpeptidation between the analogue and Ac[<sup>14</sup>C]Phe-tRNA directed to the P site through poly(U).

On the contrary, the labeled protein of the present invention is one which comprises a protein portion and a labeling compound chemically linked to a C-terminal of the protein portion.

The labeled protein of the present invention is very different from the labeled ribosome obtained by the method of Vince et al. because the analogue is not linked to the C-terminal of the ribosome.

By this feature of the present invention, the problems peculiar to the conventional labeling method using a radioactive element or a biotin-lysine-tRNA as described on page 1, line 9, to page 2, line 17 of the present specification are solved. These advantages are neither expected by nor obvious from Vince et al.

In addition, as discussed above, NAP-Lys-PAN is used as an intermediate for incorporating a radioactive label into the peptidyl transferase A. NAP-Lys-PAN itself is not used

as a label of the ribosome. Therefore, the labeling compound of the present invention is neither anticipated by nor obvious from Vince et al.

The rejection should be reconsidered and withdrawn.

Claims 13-22 have been rejected under 35 USC 103(a) as being unpatentable over Nemoto et al. (FEBS Letters, 414, 405-508) (1997)) in view of Promega Technical Bulletin No. 182.

This rejection is also respectfully traversed.

The labeled protein of the present invention relates to a molecule labeled by using a specified labeling compound. The specified labeling compound is not obvious from Nemoto et al. for the reasons discussed in the response filed September 29, 2000 with respect to the parent application. Specifically, Nemoto et al. relates to genotype assignment to phenotype (page 405, abstract), and the purpose of using the 32P-labeled rCpPur is for the confirmation of intermolecular bonding of rCpPur to the C-terminal end of the protein, as is clear from the fact that 32P-labeled rCpPur is used in combination with 35S-labeled methionine (page 406, right column, lines 5-24).

Promega Technical Bulletin merely discloses replacement of incorporation of <sup>35</sup>S-labeled methionine with incorporation of biotinylated lysine, as seen from Fig. 2 on page 2.

The combination of Nemoto et al. with Promega Technical Bulletin is untenable because mere replacement of incorporation of <sup>35</sup>S-labeled methionine with incorporation of biotinylated lysine in Nemoto et al. does not enable the confirmation of the intermolecular bonding with the advantages described in Promega Technical Bulletin.

The rejection should be reconsidered and withdrawn.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned **“Version with markings to show changes made.”**

No further issues remaining, allowance of this application is respectfully requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact undersigned at the telephone below.

Respectfully submitted,

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## **VERSION WITH MARKINGS TO SHOW CHANGES MADE**

The claims have been amended as follows:

16. (Amended) The labeled [portion] protein according to claim 15, wherein said puromycin derivative is one member selected from the group consisting of ribocytidyl puromycin, deoxycytidyl puromycin and deoxyuridyl puromycin.

22. (Amended) [A] The labeling compound [for labeling a protein, which comprises an acceptor portion] according to claim 21 wherein, said acceptor portion [comprising] comprises one member selected from the group consisting of a 3'-N-aminoacylpuromycin aminonucleoside and a 3'-N-aminoacyladenosine aminonucleoside.